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FILE 'REGISTRY' ENTERED AT 16:12:24 ON 30 JUN 2004

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STRUCTURE FILE UPDATES: 29 JUN 2004 HIGHEST RN 701199-61-3

DICTIONARY FILE UPDATES: 29 JUN 2004 HIGHEST RN 701199-61-3

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

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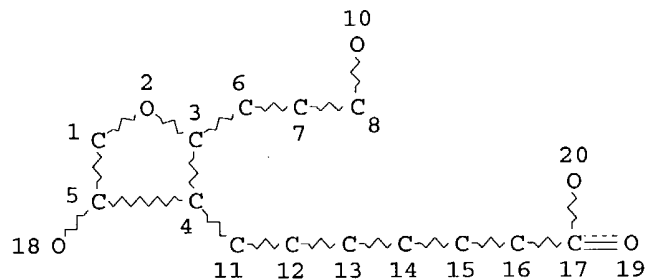
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:

<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> d que 19

L1 STR



NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC 3

NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE

L2 86 SEA FILE=REGISTRY SSS FUL L1

L6 138293 SEA FILE=REGISTRY ABB=ON PLU=ON C5-C6/ES

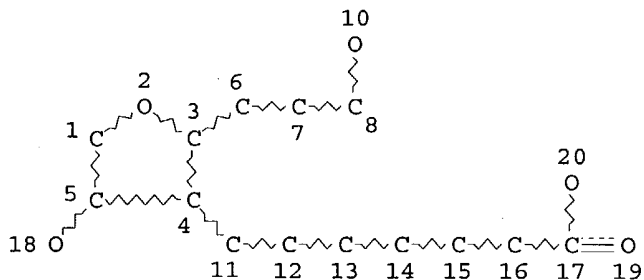
L7 2566128 SEA FILE=REGISTRY ABB=ON PLU=ON (OC4-C6 OR SC4-C6 OR NC4-C6 OR C6-C6 OR OC5-C6 OR SC5-C6 OR NC5-C6)/ES

L8 2696270 SEA FILE=REGISTRY ABB=ON PLU=ON L7 OR L6

L9 0 SEA FILE=REGISTRY ABB=ON PLU=ON L2 AND L8

=> d que 110

L1 STR



## NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

## GRAPH ATTRIBUTES:

RSPEC 3

NUMBER OF NODES IS 19

## STEREO ATTRIBUTES: NONE

L2 86 SEA FILE=REGISTRY SSS FUL L1

L10 29 SEA FILE=REGISTRY ABB=ON PLU=ON 46.150.18/RID AND L2

=&gt; b hcaplus

FILE 'HCAPLUS' ENTERED AT 16:12:49 ON 30 JUN 2004

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FILE COVERS 1907 - 30 Jun 2004 VOL 141 ISS 1

FILE LAST UPDATED: 29 Jun 2004 (20040629/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=&gt; d que l11 nos

L1 STR

L2 86 SEA FILE=REGISTRY SSS FUL L1

L10 29 SEA FILE=REGISTRY ABB=ON PLU=ON 46.150.18/RID AND L2

L11 15 SEA FILE=HCAPLUS ABB=ON PLU=ON L10

=&gt; d all fhitstr l11 1-15

L11 ANSWER 1 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:97284 HCAPLUS

DN 138:142172

ED Entered STN: 07 Feb 2003

TI Prostaglandin analogues for promotion of hair growth

IN Cagle, Gerald D.; Bergamini, Michael V. W.

PA Alcon, Inc., Switz.

SO PCT Int. Appl., 34 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K007-00

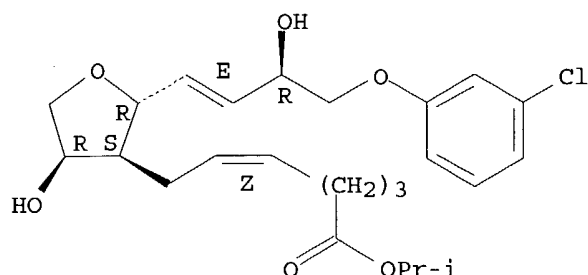
CC 62-3 (Essential Oils and Cosmetics)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003009820	A2	20030206	WO 2002-US23584	20020725
	WO 2003009820	A3	20030424		
	WO 2003009820	B1	20031113		
	W: AU, BR, CA, CN, GB, JP, MX, US				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR				
	EP 1408913	A2	20040421	EP 2002-768349	20020725
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR, BG, CZ, EE, SK				
	US 2003199590	A1	20031023	US 2002-275543	20021106
PRAI	US 2001-307835P	P	20010725		
	US 2002-373300P	P	20020417		
	WO 2002-US23584	W	20020725		
OS	MARPAT 138:142172				
AB	Methods and compns. for the promotion of hair growth in mammals, comprising PGF2 $\alpha$ analogs are disclosed. A hair growth stimulant composition contained travoprost 0.004, dextran-70 0.1, hydroxypropyl Me cellulose 0.3, NaCl 0.77, KCl 0.12, Na2EDTA 0.05, benzalkonium chlorides 0.01, HCl and/or NaOH q.s. to pH 7.2-7.5, and purified water balance to 100 %.				
ST	hair growth stimulant prostaglandin FP agonist; travoprost hair growth stimulant				
IT	Hair preparations				
	(growth stimulants; prostaglandin analogs for promotion of hair growth)				
IT	Prostanoid receptors				
	RL: BSU (Biological study, unclassified); BIOL (Biological study) (type FP; prostaglandin analogs for promotion of hair growth)				
IT	551-11-1D, PGF2 $\alpha$ , analogs	130209-82-4, Latanoprost	157283-68-6, Travoprost	192992-26-0	470455-84-6 494760-29-1
	494760-30-4 494760-31-5	494760-32-6	494760-33-7		
	RL: COS (Cosmetic use); PAC (Pharmacological activity); BIOL (Biological study); USES (Uses)				
	(prostaglandin analogs for promotion of hair growth)				
IT	192992-26-0				
	RL: COS (Cosmetic use); PAC (Pharmacological activity); BIOL (Biological study); USES (Uses)				
	(prostaglandin analogs for promotion of hair growth)				
RN	192992-26-0	HCAPLUS			
CN	L-altro-Oct-3-enitol, 5,8-anhydro-1-O-(3-chlorophenyl)-3,4,6-trideoxy-6-[(2Z)-7-(1-methylethoxy)-7-oxo-2-heptenyl]-, (3E)- (9CI) (CA INDEX NAME)				

Absolute stereochemistry.

Double bond geometry as shown.



L11 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 2002:84603 HCAPLUS  
 DN 136:129085  
 ED Entered STN: 31 Jan 2002  
 TI Use of nonsteroidal anti-inflammatory agents in combination with compounds that have FP prostaglandin agonist activity to treat glaucoma and ocular hypertension  
 IN Hellberg, Mark R.; Nixon, Jon C.  
 PA Alcon Manufacturing, Ltd., USA  
 SO U.S., 10 pp., Cont.-in-part of U.S. 6,066,671.  
 CODEN: USXXAM  
 DT Patent  
 LA English  
 IC ICM A61K031-215  
 NCL 514530000  
 CC 1-12 (Pharmacology)  
 Section cross-reference(s): 63  
 FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6342524	B1	20020129	US 2000-575833	20000522
	US 6066671	A	20000523	US 1997-994903	19971219
	PT 1039895	T	20021031	PT 1998-960732	19981204
	ES 2178291	T3	20021216	ES 1998-960732	19981204
	US 2002103255	A1	20020801	US 2002-59692	20020128
	US 6646001	B2	20031111		
PRAI	US 1997-994903	A2	19971219		
	US 2000-575833	A2	20000522		
OS	MARPAT 136:129085				
AB	Methods and comps. are provided for the treatment of glaucoma and ocular hypertension, comprising the administration of a prostaglandin analog (e.g. travoprost) and a prostaglandin synthesis inhibitor (e.g. nepafenac).				
ST	prostaglandin analog combination glaucoma ocular hypertension; prostaglandin synthesis inhibitor combination glaucoma; travoprost nepafenac glaucoma pharmaceutical				
IT	Prostaglandins				
	RL: BSU (Biological study, unclassified); BIOL (Biological study) (F, agonists; nonsteroidal anti-inflammatory agents in combination with compds. having FP prostaglandin agonist activity to treat glaucoma and ocular hypertension)				
IT	Prostaglandins				
	RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (analogs; nonsteroidal anti-inflammatory agents in combination with compds. having FP prostaglandin agonist activity to treat glaucoma and ocular hypertension)				

- IT Antiglaucoma agents  
(nonsteroidal anti-inflammatory agents in combination with compds.  
having FP prostaglandin agonist activity to treat glaucoma and ocular  
hypertension)
- IT Anti-inflammatory agents  
(nonsteroidal; nonsteroidal anti-inflammatory agents in combination  
with compds. having FP prostaglandin agonist activity to treat glaucoma  
and ocular hypertension)
- IT Drug delivery systems  
(ophthalmic; nonsteroidal anti-inflammatory agents in combination with  
compds. having FP prostaglandin agonist activity to treat glaucoma and  
ocular hypertension)
- IT 78281-72-8, Nepafenac 78281-73-9 78281-77-3 120373-36-6, Unoprostone  
130209-82-4, Latanoprost 157283-68-6, Travoprost 192992-28-2  
392230-89-6 392230-90-9  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(nonsteroidal anti-inflammatory agents in combination with compds.  
having FP prostaglandin agonist activity to treat glaucoma and ocular  
hypertension)

RE.CNT 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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- (2) Akarsu; Human Molecular Genetics 1996, V5(8), P1199 HCAPLUS
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- (7) Anon; WO 9208465 1992 HCAPLUS
- (8) Anon; WO 9517178 1995 HCAPLUS
- (9) Anon; WO 9614411 1996 HCAPLUS
- (10) Anon; WO 9640102 1996 HCAPLUS
- (11) Anon; WO 9640103 1996 HCAPLUS
- (12) Anon; WO 0025771 2000 HCAPLUS
- (13) Bishop; US 5510383 A 1996 HCAPLUS
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- (40) Sallee; US 5721273 A 1998 HCAPLUS
- (41) Sallman; US 6107343 A 2000 HCAPLUS
- (42) Sarfarazi; Genomics 1995, V30, P171 HCAPLUS
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- (46) Selliah; US 5994397 A 1999 HCAPLUS
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- (49) Sommer, A; Arch Ophthalmol 1991, V109, P1090 MEDLINE
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- (52) Stone; Science 1997, V275, P668 HCAPLUS
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- (54) Ueno; US 5151444 A 1992 HCAPLUS
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- (58) Woodward; US 5093329 A 1992 HCAPLUS
- (59) Yanni; US 5475034 A 1995 HCAPLUS
- (60) Yanni; US 6066671 A 2000 HCAPLUS
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- (62) Zinke; US 6172109 B1 2001 HCAPLUS

IT 192992-28-2

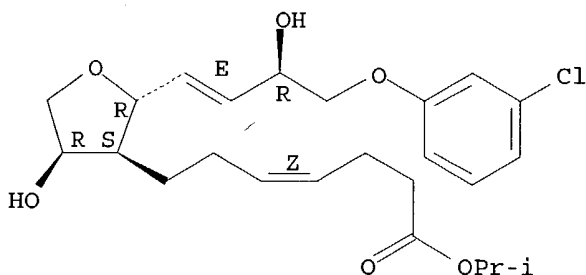
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)

(nonsteroidal anti-inflammatory agents in combination with compds.  
having FP prostaglandin agonist activity to treat glaucoma and ocular  
hypertension)

RN 192992-28-2 HCAPLUS

CN L-alto-Oct-3-enitol, 5,8-anhydro-1-O-(3-chlorophenyl)-3,4,6-trideoxy-6-  
[(3Z)-7-(1-methylethoxy)-7-oxo-3-heptenyl]-, (3E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).  
Double bond geometry as shown.



L11 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:11126 HCAPLUS

DN 136:85723

ED Entered STN: 04 Jan 2002

TI Process and preparation of novel intermediates for an 11-oxa prostaglandin

IN Delgado, Pete; Conrow, Raymond E.; Dean, William D.; Gaines, Michael S.

PA USA

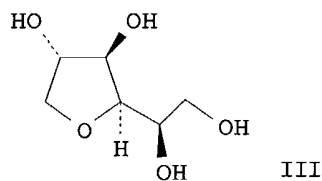
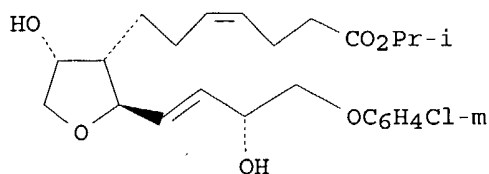
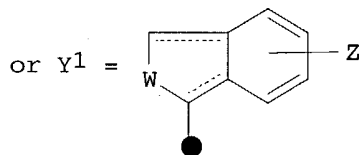
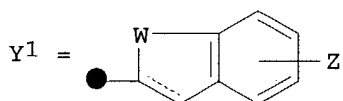
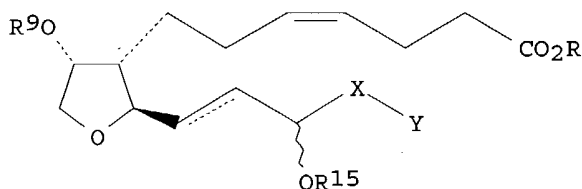
SO U.S. Pat. Appl. Publ., 12 pp.

CODEN: USXXCO

DT Patent

LA English  
 IC ICM C07D409-02  
 ICS C07D333-72; C07D037-32  
 NCL 546152000  
 CC 26-3 (Biomolecules and Their Synthetic Analogs)  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002002284	A1	20020103	US 2001-860772	20010518
	US 6441196	B2	20020827		
	US 2003013884	A1	20030116	US 2002-227912	20020826
	US 6620947	B2	20030916		
	US 2004063968	A1	20040401	US 2003-663855	20030916
PRAI	US 2000-205692P	P	20000519		
	US 2001-860772	A1	20010518		
	US 2002-227912	A1	20020826		
OS	CASREACT 136:85723; MARPAT 136:85723				
GI					

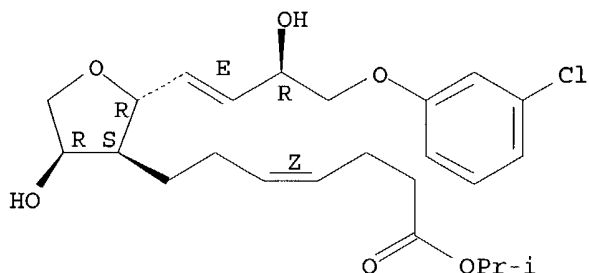


AB Improved processes and intermediates for preparation of 11-oxa prostaglandin analogs I (R = H, pharmaceutically acceptable cationic salt moiety, or CO2R forms a pharmaceutically acceptable ester moiety; R9O and R15O = same or different and constitute a free or functionally modified hydroxy group; --- = single or trans double bond; X = (CH2)<sub>p</sub> or (CH2)<sub>p</sub>O where p = 1-6; Y = (substituted)phenyl ring; or X-Y = (CH2)<sub>m</sub>Y1 where m = 0-6 and W = CH2, O, S(O)<sub>x</sub>, NR10, CH2CH2, CH=CH, CH2O, CH2S(O)<sub>x</sub>, CH=N, CH2NR10 where x = 0-2 and R10 = H, alkyl, acyl; Z = H, alkyl, alkoxy, acyl(oxy), halo, amino, OH) were accomplished. Thus II was prepared in 90% yield from D-sorbitol via III in a multistep process.

ST oxaprostaglandin analog prepn; prostaglandin oxa analog prepn; heptenoate tetrahydrofuranhydroxy analog prepn; furan hydroxytetrahydro heptenoic

acid deriv prepn  
 IT Prostaglandins  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (analog, 11-oxa; preparation of 11-oxa prostaglandin analogs)  
 IT **192992-28-2P** 385842-08-0P **385842-09-1P**  
 RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of 11-oxa prostaglandin analogs)  
 IT 50-70-4, D-Sorbitol, reactions 67-63-0, 2-Propanol, reactions 77-76-9, 2,2-Dimethoxypropane 108-43-0, 3-Chlorophenol 534-07-6, 1,3-Dichloroacetone 1099-45-2 2623-87-2, 4-Bromobutyric acid 40665-94-9, Dimethyl 3-(3-chlorophenoxy)-2-oxopropyl phosphonate  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (preparation of 11-oxa prostaglandin analogs)  
 IT 13605-65-7P 13605-66-8P 27299-12-3P 70923-64-7P, Isopropyl 4-bromobutyrate 73718-87-3P 101069-27-6P 101069-28-7P 101125-99-9P 159898-26-7P 256662-69-8P 374680-98-5P **374680-99-6P** 385841-95-2P 385841-96-3P 385841-97-4P 385841-98-5P 385841-99-6P 385842-00-2P 385842-01-3P 385842-02-4P 385842-03-5P 385842-04-6P 385842-05-7P 385842-06-8P **385842-07-9P**  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of 11-oxa prostaglandin analogs)  
 IT **192992-28-2P**  
 RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of 11-oxa prostaglandin analogs)  
 RN 192992-28-2 HCAPLUS  
 CN L-altro-Oct-3-enitol, 5,8-anhydro-1-O-(3-chlorophenyl)-3,4,6-trideoxy-6-[(3Z)-7-(1-methylethoxy)-7-oxo-3-heptenyl]-, (3E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).  
 Double bond geometry as shown.



L11 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 2001:851169 HCAPLUS  
 DN 135:371564  
 ED Entered STN: 23 Nov 2001  
 TI Process for preparing 11-oxaprostaglandins and intermediates  
 IN Fox, Martin Edward; Jackson, Mark  
 PA Chirotech Technology Limited, UK  
 SO PCT Int. Appl., 26 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM C07F007-18

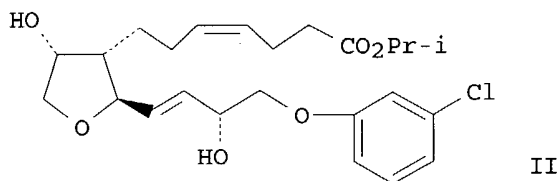
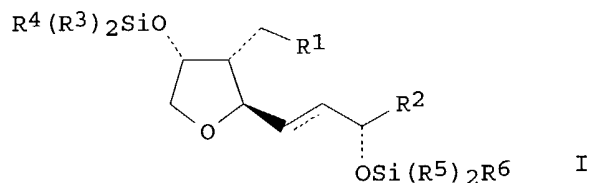
Searched by P. Ruppel



CC 26-3 (Biomolecules and Their Synthetic Analogs)

FAN: CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001087897	A1	20011122	WO 2001-GB2184	20010516
	W: CA, JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
	EP 1282627	A1	20030212	EP 2001-936608	20010516
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
	US 2003166948	A1	20030904	US 2003-276846	20030505
PRAI	GB 2000-12249	A	20000519		
	WO 2001-GB2184	W	20010516		
OS	CASREACT 135:371564; MARPAT 135:371564				
GI					



AB The present invention discloses a process for the preparation of 11-oxaprostaglandin derivs. [I; R1 = vinyl, trialkylsilylethynyl, formyl protected as an acetal, protected hydroxymethyl group; R2 = alkyl, aryloxy, alkoxy; R3-R6 = alkyl, aryl; dashed bond = single or double bond] and intermediates thereof. Thus, oxaprostaglandin derivative II was prepared via multistep synthetic sequence starting from Me (R)-(4-tert-butyl dimethylsilyloxy)-3-hydroxybutanoate, trimethylsilylpropargyl bromide, allyl bromide and (E)-1-iodo-4-(3-chlorophenoxy)-3-tert-butyl dimethylsilyloxy-1-butene.

ST prostaglandin oxa intermediate prepn

IT Asymmetric synthesis and induction  
(of 11-oxaprostaglandins and intermediates)

IT Prostaglandins  
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)  
(preparation of 11-oxaprostaglandins and intermediates)

IT Coupling reaction  
(stereoselective; in preparation of 11-oxaprostaglandins and intermediates)

IT 15489-27-7  
RL: CAT (Catalyst use); USES (Uses)

(preparation of 11-oxaprostaglandins and intermediates)

IT 256662-69-8P 374680-85-0P 374680-86-1P 374680-87-2P 374680-88-3P  
 374680-89-4P 374680-90-7P 374680-91-8P 374680-92-9P 374680-93-0P  
 374680-94-1P 374680-95-2P 374680-96-3P 374680-97-4P 374680-98-5P  
**374680-99-6P**  
 RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of 11-oxaprostaglandins and intermediates)

IT **192992-28-2P** 374681-02-4P  
 RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of 11-oxaprostaglandins and intermediates)

IT 75-77-4, Trimethylsilyl chloride, reactions 106-95-6, Allyl bromide, reactions 603-35-0, Triphenylphosphine, reactions 18162-48-6  
 38002-45-8, Trimethylsilylpropargyl bromide 40949-94-8, Potassiumbis(trimethylsilyl)amide 70923-64-7, Isopropyl 4-bromobutyrate 133095-91-7 374681-00-2 374681-01-3 374681-03-5  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (preparation of 11-oxaprostaglandins and intermediates)

IT 374681-04-6P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of 11-oxaprostaglandins and intermediates)

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD

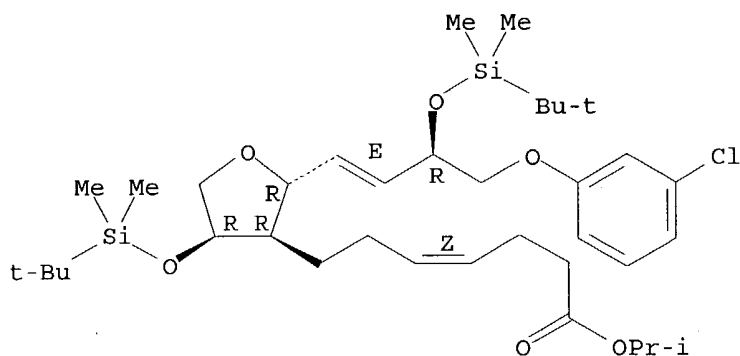
RE  
 (1) Alcon Lab Inc; WO 9723223 A 1997 HCAPLUS  
 (2) Alcon Lab Inc; WO 9821182 A 1998 HCAPLUS

IT **374680-99-6P**  
 RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of 11-oxaprostaglandins and intermediates)

RN 374680-99-6 HCAPLUS

CN L-alto-Oct-3-enitol, 5,8-anhydro-1-O-(3-chlorophenyl)-3,4,6-trideoxy-2,7-bis-O-[(1,1-dimethylethyl)dimethylsilyl]-6-[(3Z)-7-(1-methylethoxy)-7-oxo-3-heptenyl]-, (3E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).  
 Double bond geometry as shown.



L11 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 2000:114400 HCAPLUS  
 DN 132:151597  
 ED Entered STN: 17 Feb 2000  
 TI Preparation and formulation of tetrahydrofuran prostaglandin analogs for use as ocular hypotensives

Searched by P. Ruppel

IN Selliah, Robert D.; Hellberg, Mark R.; Klimko, Peter G.; Sallee, Verney L.; Zinke, Paul W.

PA Alcon Laboratories, Inc., USA

SO U.S., 12 pp., Cont.-in-part of U.S. Ser. No. 809,920.

CODEN: USXXAM

DT Patent

LA English

IC ICM A61K031-34

ICS C07D307-20

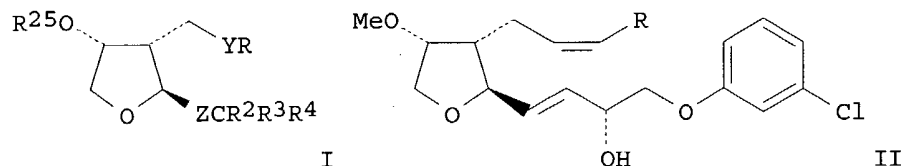
NCL 514473000

CC 26-3 (Biomolecules and Their Synthetic Analogs)

Section cross-reference(s): 1, 2, 63

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6025392	A	20000215	US 1998-109852	19980702
	WO 9723223	A1	19970703	WO 1996-US17900	19961112
	W: AU, CA, CN, JP, MX, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5994397	A	19991130	US 1997-809920	19970404
PRAI	US 1995-9866P	P	19951222		
	WO 1996-US17900	W	19961112		
	US 1997-809920	A2	19970404		
OS	MARPAT 132:151597				
GI					



AB THF analogs of F-series prostaglandins, such as I [R = carboxyalkyl, amidoalkyl, hydroxyalkyl, etc.; R2, R3 = H, F, OH, etc.; R4 = phenoxyalkyl, phenylalkyl, etc.; R25 = H, acyl, alkyl; Y = cis-CH2CH:CH, cis-CH:CHCH2, (CH2)3; Z = C.tplbond.C, trans-CH:CH, (CH2)2], were prepared for use in treating glaucoma and ocular hypertension. Thus, THF prostanoids II (R = (CH2)nCO2CHMe2, n = 2, 3) were both prepared in a multistep synthetic sequence starting from 1,2-O-isopropylidene- $\alpha$ -D-xylofuranose. A formulation for eye drops containing II (R = (CH2)2CO2CHMe2) was presented.

ST THF prostaglandin analog prepn antiglaucoma agent; ocular hypotensive THF prostaglandin analog prepn

IT Antiglaucoma agents  
(preparation and formulation of THF prostaglandin analogs for use as ocular hypotensives)

IT Prostaglandins  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prostanoids; preparation and formulation of THF prostaglandin analogs for use as ocular hypotensives)

IT 257945-30-5P 257945-31-6P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation and formulation of THF prostaglandin analogs for use as ocular hypotensives)

IT 867-13-0, Triethyl phosphonoacetate 4009-98-7,  
(Methoxymethyl)triphenylphosphonium chloride 17814-85-6 17857-14-6  
20031-21-4 40665-94-9  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation and formulation of THF prostaglandin analogs for use as ocular hypotensives)

IT 6022-96-4P 6698-46-0P 58399-68-1P 80923-96-2P 192991-91-6P  
192991-92-7P 192991-93-8P 192991-94-9P 192991-95-0P 192991-98-3P  
192992-00-0P 192992-02-2P **192992-03-3P** 193075-40-0P  
208180-29-4P 208180-30-7P 208180-62-5P 242812-26-6P 242812-27-7P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and formulation of THF prostaglandin analogs for use as ocular hypotensives)

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

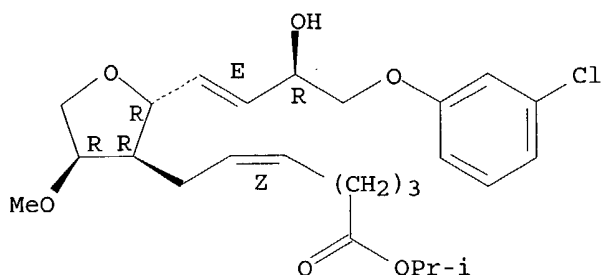
- (1) Alm; Current Opinion in Ophthalmology 1993, V4(II), P44
- (2) Anon; GB 1458164 1976 HCAPLUS
- (3) Anon; DE 2460977 1976 HCAPLUS
- (4) Anon; DE 2601333 1976 HCAPLUS
- (5) Anon; DE 2618861 1976 HCAPLUS
- (6) Anon; DE 2739277 1978 HCAPLUS
- (7) Anon; GB 1539364 1979 HCAPLUS
- (8) Anon; EP 0667160 A2 1995 HCAPLUS
- (9) Anon; EP 0686628 A2 1995 HCAPLUS
- (10) Anon; WO 9526729 1995 HCAPLUS
- (11) Arndt; Afr J Chem 1981, V34(4), P121 HCAPLUS
- (12) Chan; US 5574066 1996 HCAPLUS
- (13) Giuffre; Graefe's Arch Clin Exp Ophthalmol 1985, V222, P139 MEDLINE
- (14) Hanessian; Carbohydrate Research 1985, V141, P221 HCAPLUS
- (15) Kerstetter; American Journal of Ophthalmology 1988, V105, P30 HCAPLUS
- (16) Lourens; US 4133817 1979 HCAPLUS
- (17) Lourens; Tetrahedron Letters 1975, V43, P3719
- (18) Nakajima; Graefe's Arch Clin Exp Ophthalmol 1991, V229, P411 MEDLINE
- (19) Thiem; Liebigs Ann Chem 1985, V2151, P2164
- (20) Thierauch; Journal of Hypertension 1994, V12, P1 HCAPLUS
- (21) Verdoorn; S Afr Tydskr Chem 1987, V40(2), P134 HCAPLUS
- (22) Vlattas; US 3883659 1975 HCAPLUS
- (23) Vlattas; US 4088779 1978 HCAPLUS
- (24) Vlattas; Tetrahedron Letters 1974, 51/52, P4451 HCAPLUS
- (25) Vlattas; Tetrahedron Letters 1974, 51/52, P4455 HCAPLUS

IT **257945-30-5P**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation and formulation of THF prostaglandin analogs for use as ocular hypotensives)

RN 257945-30-5 HCAPLUS

CN L-altro-Oct-3-enitol, 5,8-anhydro-1-O-(3-chlorophenyl)-3,4,6-trideoxy-7-O-methyl-6-[(2Z)-7-(1-methylethoxy)-7-oxo-2-heptenyl]-, (3E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



L11 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 2000:84616 HCAPLUS  
 DN 132:141953  
 ED Entered STN: 04 Feb 2000  
 TI Ophthalmic compositions containing prostaglandins and carbonic anhydrase inhibitors for treatment of ocular hypertension  
 IN Ponticello, Gerald S.; Sugrue, Michael F.  
 PA Merck & Co., Inc., USA  
 SO PCT Int. Appl., 29 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM A61K031-215  
 CC 63-6 (Pharmaceuticals)  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000004899	A1	20000203	WO 1999-US16374	19990720
W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2337349	AA	20000203	CA 1999-2337349	19990720
AU 9951144	A1	20000214	AU 1999-51144	19990720
EP 1100491	A1	20010523	EP 1999-935726	19990720
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002521333	T2	20020716	JP 2000-560892	19990720
PRAI US 1998-119951	A	19980721		
WO 1999-US16374	W	19990720		

AB Combinations of a prostaglandin, or its derivative, hypotensive lipids derived from a prostaglandin or prostaglandin derivative or an ophthalmol. acceptable salt and a topical carbonic anhydrase inhibitors or their salts are particularly useful in the treatment of ocular hypertension and glaucoma. The combinations are characterized by an improved effect and reduced side-effects. Thus, a solution contained (S,S)-(-)-5,6-dihydro-4-ethylamino-6-methyl-4H-thieno-[2,3b]thiopyran-2-sulfonamide-7,7-dioxide monohydrochloride (carbonic anhydrase inhibitor) 22.26, (+)-isopropylfluprostenol (prostaglandin derivative) 10.0, sodium citrate-2H<sub>2</sub>O 2.940, benzalkonium chloride 0.075, hydroxyethyl cellulose 5.00, sodium hydroxide qs to pH 6.0, mannitol 16.00, and water for injection qs to 1000 g.

ST ophthalmic prostaglandin carbonic anhydrase inhibitor; ocular hypertension

prostaglandin carbonic anhydrase inhibitor

IT Antiglaucoma agents  
(ophthalmic compns. containing prostaglandins and carbonic anhydrase inhibitors for treatment of ocular hypertension)

IT Prostaglandins  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(ophthalmic compns. containing prostaglandins and carbonic anhydrase inhibitors for treatment of ocular hypertension)

IT Drug delivery systems  
(ophthalmic; ophthalmic compns. containing prostaglandins and carbonic anhydrase inhibitors for treatment of ocular hypertension)

IT Lipids, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(prostaglandin-derived; ophthalmic compns. containing prostaglandins and carbonic anhydrase inhibitors for treatment of ocular hypertension)

IT 9001-03-0, Carbonic anhydrase  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitor; ophthalmic compns. containing prostaglandins and carbonic anhydrase inhibitors for treatment of ocular hypertension)

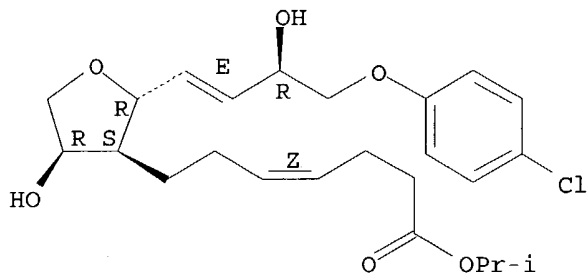
IT 11138-66-2, Xanthan gum 13345-50-1, Prostaglandin A2 14152-28-4  
27376-76-7 38562-01-5 53764-90-2 71010-52-1, Gellan gum  
120279-96-1 120373-16-2 120373-24-2 122028-16-4 130693-82-2  
135273-39-1 138890-50-3 138890-62-7 138890-75-2 138890-81-0  
139066-78-7 141115-93-7 216854-98-7 246145-93-7 **256926-02-0**  
256944-51-1  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(ophthalmic compns. containing prostaglandins and carbonic anhydrase inhibitors for treatment of ocular hypertension)

IT **256926-02-0**  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(ophthalmic compns. containing prostaglandins and carbonic anhydrase inhibitors for treatment of ocular hypertension)

RN 256926-02-0 HCAPLUS

CN L-alto-Oct-3-enitol, 5,8-anhydro-1-O-(4-chlorophenyl)-3,4,6-trideoxy-6-[(3Z)-7-(1-methylethoxy)-7-oxo-3-heptenyl]-, (3E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



L11 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN  
AN 2000:84614 HCAPLUS  
DN 132:127751  
ED Entered STN: 04 Feb 2000  
TI Ophthalmic compositions containing carbonic anhydrase inhibitor,  $\beta$ -adrenergic antagonist, and prostaglandin for treating ocular hypertension  
IN Ponticello, Gerald S.; Sugrue, Michael F.

PA Merck & Co., Inc., USA  
 SO PCT Int. Appl., 34 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC A61K031-215  
 CC 63-6 (Pharmaceuticals)  
 Section cross-reference(s): 1

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000004898	A1	20000203	WO 1999-US16143	19990716
	W:	AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GN, GW, ML, MR, NE, SN, TD, TG			
	CA 2337399	AA	20000203	CA 1999-2337399	19990716
	AU 9950011	A1	20000214	AU 1999-50011	19990716
	EP 1109546	A1	20010627	EP 1999-934101	19990716
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
	JP 2002521332	T2	20020716	JP 2000-560891	19990716
PRAI	US 1998-93594P	P	19980721		
	WO 1999-US16143	W	19990716		
OS	MARPAT 132:127751				
AB	Combinations of a carbonic anhydrase inhibitor (0.5-3.0%), a $\beta$ -adrenergic antagonist (0.1-0.5%), and a prostaglandin or a prostaglandin derivative (0.03-1.0%) are particularly useful in the treatment of ocular hypertension (glaucoma). The combinations are characterized by an improved therapeutic effect and reduced side-effects. E.g., an ophthalmic formulation was prepared containing a carbonic anhydrase inhibitor, MK 507, 22.26 g, 13,14-dihydro-15-keto-20-ethyl-PGF2 iso-Pr ester 10 g, (S)-(-)-(tert-butylamino)-3-[(4-morpholino-1,2,5-thiadiazol-3-yl)oxy]-2-propanol maleate 6.834 g, Na citrate·2H <sub>2</sub> O 2.940 g, benzalkonium chloride 0.075 g, hydroxyethyl cellulose 5.00 g, NaOH as needed for pH = 6.0, mannitol 16.00 g, and water for injection up to 1000 g. The active compds., phosphate buffer salts, benzalkonium chloride, and Polysorbate 80 were added to and suspended or dissolved in water. The pH of the composition was adjusted to 5.5-6.0 and diluted 30 to volume. The composition was rendered sterile by filtration through a sterilizing filter.				
ST	anhydrase inhibitor beta blocker prostaglandin ophthalmic glaucoma;				
IT	Antiglaucoma agents				
	(ophthalmic compns. containing anhydrase inhibitor, $\beta$ -blocker, and prostaglandin for glaucoma treatment)				
IT	Prostaglandins				
	RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)				
	(ophthalmic compns. containing anhydrase inhibitor, $\beta$ -blocker, and prostaglandin for glaucoma treatment)				
IT	Drug delivery systems				
	(ophthalmic; ophthalmic compns. containing anhydrase inhibitor, $\beta$ -blocker, and prostaglandin for glaucoma treatment)				
IT	Drug delivery systems				
	(solns., ophthalmic; ophthalmic compns. containing anhydrase inhibitor, $\beta$ -blocker, and prostaglandin for glaucoma treatment)				

IT Drug delivery systems  
(suspensions, ophthalmic; ophthalmic compns. containing anhydrase inhibitor,  $\beta$ -blocker, and prostaglandin for glaucoma treatment)

IT Adrenoceptor antagonists  
( $\beta$ -; ophthalmic compns. containing anhydrase inhibitor,  $\beta$ -blocker, and prostaglandin for glaucoma treatment)

IT 9001-03-0, Carbonic anhydrase  
RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; ophthalmic compns. containing anhydrase inhibitor,  $\beta$ -blocker, and prostaglandin for glaucoma treatment)

IT 13345-50-1, PGA2 14152-28-4, PGA1 22664-55-7, Metipranolol 26839-75-8, Timolol 33305-95-2 35850-13-6 38562-01-5, Prostaglandin F2 $\alpha$  tromethamine salt 39552-01-7, Befunolol 41639-83-2D, esters 47141-42-4, Levobunolol 51781-06-7, Carteolol 53764-90-2 58581-22-9 63659-18-7, Betaxolol 118565-33-6 120279-96-1 120373-24-2 120373-36-6 130209-82-4 130693-82-2 134217-11-1 135273-39-1 138890-62-7 138890-84-3 139066-78-7 157283-68-6 161833-99-4 162478-72-0 164582-55-2 179937-10-1 **192992-28-2** 216780-87-9 216780-88-0 216780-89-1 256444-30-1  
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (ophthalmic compns. containing anhydrase inhibitor,  $\beta$ -blocker, and prostaglandin for glaucoma treatment)

IT 11138-66-2, Xanthan gum 71010-52-1, Gellan gum  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (ophthalmic compns. containing anhydrase inhibitor,  $\beta$ -blocker, and prostaglandin for glaucoma treatment)

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD

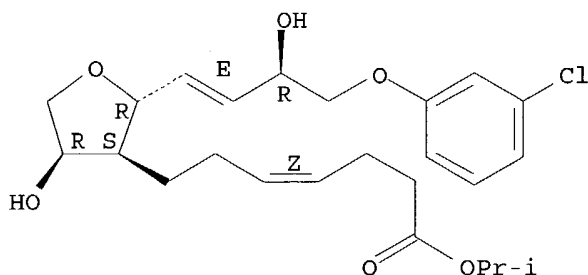
RE  
(1) Bito; US 4599353 A 1986 HCAPLUS

IT **192992-28-2**  
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (ophthalmic compns. containing anhydrase inhibitor,  $\beta$ -blocker, and prostaglandin for glaucoma treatment)

RN 192992-28-2 HCAPLUS

CN L-altro-Oct-3-enitol, 5,8-anhydro-1-O-(3-chlorophenyl)-3,4,6-trideoxy-6-[(3Z)-7-(1-methylethoxy)-7-oxo-3-heptenyl]-, (3E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).  
Double bond geometry as shown.



L11 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN  
AN 2000:10635 HCAPLUS  
DN 132:69332

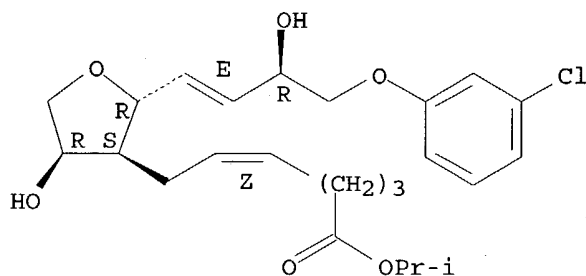


ED Entered STN: 06 Jan 2000  
 TI Storage-stable prostaglandin compositions  
 IN Schneider, L. Wayne; Bawa, Rajan; Weiner, Alan L.  
 PA Alcon Laboratories, Inc., USA  
 SO U.S., 11 pp., Cont.-in-part of U.S. Ser. No. 33,748, abandoned.  
 CODEN: USXXAM  
 DT Patent  
 LA English  
 IC ICM A61K031-557  
 NCL 514530000  
 CC 63-6 (Pharmaceuticals)  
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6011062	A	20000104	US 1999-246072	19990209
	US 5631287	A	19970520	US 1994-362677	19941222
	US 5849792	A	19981215	US 1996-738629	19961029
PRAI	US 1994-362677	A3	19941222		
	US 1996-738629	A2	19961029		
	US 1998-33748	B2	19980224		
AB	Polyethoxylated castor oils are used in prostaglandin compns. to enhance the chemical stability. A composition was prepared containing				
(5Z)	-(9R,11R,15R)-9-chloro-15-cyclohexyl-11,15-dihydroxy-3-oxa-16,17,18,19,20-pentanor-5-prostenoic acid iso-Pr ester and Cremophor EL.				
ST	prostaglandin compn ethoxylated castor oil				
IT	Castor oil				
	RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)				
	(ethoxylated; storage-stable prostaglandin compns. containing ethoxylated castor oil)				
IT	Castor oil				
	RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)				
	(hydrogenated, ethoxylated; storage-stable prostaglandin compns. containing ethoxylated castor oil)				
IT	Polyoxyalkylenes, biological studies				
	RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)				
	(storage-stable prostaglandin compns. containing ethoxylated castor oil)				
IT	Prostaglandins				
	RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)				
	(storage-stable prostaglandin compns. containing ethoxylated castor oil)				
IT	25322-68-3				
	RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)				
	(storage-stable prostaglandin compns. containing ethoxylated castor oil)				
IT	53764-90-2, PGF2 $\alpha$ isopropyl ester 130209-82-4, Latanoprost				
	135646-98-9, 15-Ketolatanoprost 155206-02-3 157283-66-4, Cloprostenol				
	isopropyl ester 163075-20-5 170291-05-1 170291-06-2 170291-07-3				
	170291-08-4	170291-11-9	170291-13-1	170552-18-8	170552-20-2
	190951-81-6	190951-85-0	190951-87-2	190951-89-4	190951-91-8
	190951-93-0	190951-94-1	190951-95-2	190951-96-3	190951-97-4
	190951-98-5	190951-99-6	190952-00-2	190952-01-3	190952-02-4
	190952-03-5	192992-26-0	246145-93-7	253436-50-9	
	253436-51-0				
	RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)				
	(storage-stable prostaglandin compns. containing ethoxylated castor oil)				
RE.CNT	23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD				
RE					

(1) Anon; WO 8502841 1984 HCAPLUS  
 (2) Anon; EP 0132027 A1 1985 HCAPLUS  
 (3) Anon; EP 0330511 A2 1989 HCAPLUS  
 (4) Anon; EP 0407148 A3 1991  
 (5) Anon; EP 0418004 A2 1991 HCAPLUS  
 (6) Anon; EP 0429248 A2 1991 HCAPLUS  
 (7) Anon; EP 0435682 A2 1991 HCAPLUS  
 (8) Anon; EP 0645145 A3 1995 HCAPLUS  
 (9) Anon; EP 0667160 A2 1995 HCAPLUS  
 (10) Anon; WO 9505163 1995 HCAPLUS  
 (11) Anon; WO 9729752 1997 HCAPLUS  
 (12) Anon; WO 9841208 1998 HCAPLUS  
 (13) Attwood; Surfactant Systems Their Chemistry Pharmacy and Biology V11, P698  
 (14) Cherng-Chyi; US 5110493 1992 HCAPLUS  
 (15) DeSantis; US 5627209 1997 HCAPLUS  
 (16) Foster; Arch Ophthalmol 1979, V97/9, P1703  
 (17) Joose; US 4075333 1978 HCAPLUS  
 (18) Nagy; US 4960799 1990 HCAPLUS  
 (19) Nakajima; US 5098606 1992 HCAPLUS  
 (20) Sayed; Interna'l J of Pharmaceutics 1983, V13, P302  
 (21) Schneider; US 5631287 1997 HCAPLUS  
 (22) Schneider; US 5849792 1998 HCAPLUS  
 (23) Ushio; US 5185372 1993 HCAPLUS  
 IT 192992-26-0  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (storage-stable prostaglandin compns. containing ethoxylated castor oil)  
 RN 192992-26-0 HCAPLUS  
 CN L-alto-Oct-3-enitol, 5,8-anhydro-1-O-(3-chlorophenyl)-3,4,6-trideoxy-6-  
 [(2Z)-7-(1-methylethoxy)-7-oxo-2-heptenyl]-, (3E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



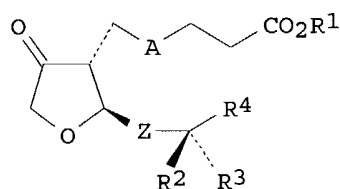
L11 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1999:9814 HCAPLUS  
 DN 130:66325  
 ED Entered STN: 07 Jan 1999  
 TI Keto-substituted tetrahydrofuran analogs of prostaglandins as ocular  
 hypotensives  
 IN Selliah, Robert D.  
 PA Alcon Laboratories, Inc., USA  
 SO PCT Int. Appl., 27 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM C07C405-00  
 ICS A61K031-557

CC 26-3 (Biomolecules and Their Synthetic Analogs)

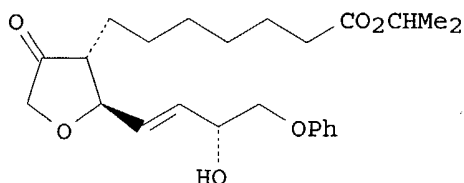
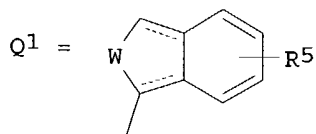
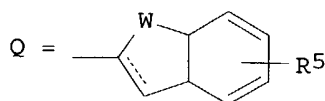
Section cross-reference(s): 1, 63

FAN.CNT 1

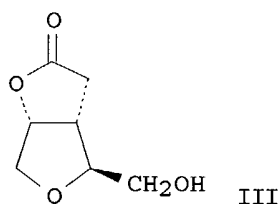
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9857930	A1	19981223	WO 1998-US11340	19980603
	W: AU, BR, CA, JP, MX, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5866602	A	19990202	US 1997-878031	19970618
	AU 9878101	A1	19990104	AU 1998-78101	19980603
PRAI	US 1997-878031		19970618		
	WO 1998-US11340		19980603		
OS	MARPAT 130:66325				
GI					



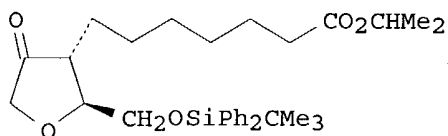
I



II



III



IV

AB Keto-substituted THF analogs of prostaglandins I ( $R_1 = H$ , C1-5-alkyl, C3-6-cycloalkyl, cationic salt moiety;  $A = CH_2CH=CH$  (cis olefin),  $CH=CHCH_2$  (cis olefin),  $CH_2CH_2CH_2$ ;  $Z = C.tplbond.C$ , trans- $CH=CH$ ; one of  $R_2$  and  $R_3 = H$  and the other = F or OH, the OH may be free or functionally modified;  $R_2R_3 = OCH_2CH_2O$ , O;  $R_4 = (CH_2)_mXPh$ ,  $(CH_2)_pZ$ ;  $m = 1-6$ ,  $X = O$ ,  $CH_2$ , the Ph may be substituted with  $R_5$ ,  $R_5 = halo$ , Me,  $CF_3$ , cyano, MeO, acetyl;  $p = 0-6$ ,  $Z = Q$ ,  $Q_1$ ;  $W = O$ ,  $CH_2$ ,  $CH_2CH_2$ ,  $CH=CH$ ) were prepared for treatment of glaucoma and ocular hypertension. Thus the tetrahydrofuranyleptanoate derivative II was prepared in 8 steps from the alc. III via the tetrahydrofuranyleptanoate derivative IV. Pharmaceutical formulations containing 0.01 and 0.003 wt% II were prepared

ST furanylheptanoate tetrahydro prepn ocular hypotensive;  
tetrahydrofuranyleptanoate prepn ocular hypotensive; THF prostaglandin analog prepn ocular hypotensive

IT Antiglaucoma agents  
 Glaucoma (disease)  
 (preparation of keto-substituted THF analogs of prostaglandins as ocular hypotensives)

IT Prostaglandins  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of keto-substituted THF analogs of prostaglandins as ocular hypotensives)

IT **217939-71-4P 217939-72-5P**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (preparation of keto-substituted THF analogs of prostaglandins as ocular hypotensives)

IT 17814-85-6, (4-Carboxybutyl)triphenylphosphonium bromide 40665-68-7, Dimethyl 3-phenoxy-2-oxopropylphosphonate 192991-95-0  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (preparation of keto-substituted THF analogs of prostaglandins as ocular hypotensives)

IT 208180-29-4P 217939-65-6P 217939-66-7P 217939-67-8P 217939-68-9P 217939-69-0P 217939-70-3P 217939-73-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of keto-substituted THF analogs of prostaglandins as ocular hypotensives)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

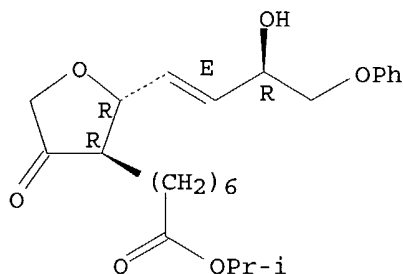
RE  
 (1) Chembro Holdings PTY Ltd; DE 2618861 A 1976 HCAPLUS  
 (2) Pfizer; GB 1539364 A 1979 HCAPLUS  
 (3) Stjernschantz, J; WO 9526729 A 1995 HCAPLUS

IT **217939-71-4P**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (preparation of keto-substituted THF analogs of prostaglandins as ocular hypotensives)

RN 217939-71-4 HCAPLUS

CN L-lyxo-Oct-5-en-2-ulose, 1,4-anhydro-3,5,6-trideoxy-3-[7-(1-methylethoxy)-7-oxoheptyl]-8-O-phenyl-, (5E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).  
 Double bond geometry as shown.



L11 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1998:341542 HCAPLUS  
 DN 129:41028  
 ED Entered STN: 06 Jun 1998  
 TI Preparation of cis- $\Delta$ 4 analogs of prostaglandins as ocular  
 hypotensives  
 IN Klimko, Peter G.; Zinke, Paul W.  
 PA Alcon Laboratories, Inc., USA; Klimko, Peter G.; Zinke, Paul W.  
 SO PCT Int. Appl., 48 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM C07C405-00  
 CC 26-3 (Biomolecules and Their Synthetic Analogs)  
 Section cross-reference(s): 2, 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9821182	A2	19980522	WO 1997-US20857	19971107
	WO 9821182	A3	19980625		
	W: AU, CA, CN, JP, KR, MX, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9854393	A1	19980603	AU 1998-54393	19971107
	EP 944593	A2	19990929	EP 1997-948304	19971107
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	CN 1237157	A	19991201	CN 1997-199645	19971107
	JP 2001504122	T2	20010327	JP 1998-522859	19971107
	KR 2000053228	A	20000825	KR 1999-704203	19990512
	BR 9901566	A	20010109	BR 1999-1566	19990520
	US 6235779	B1	20010522	US 1999-284431	19990602
PRAI	US 1996-30504P	P	19961112		
	WO 1997-US20857	W	19971107		
OS	MARPAT 129:41028				
GI					

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

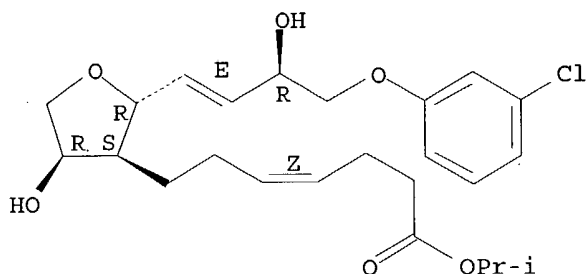
AB Cis- $\Delta$ 4 analogs of prostaglandins I (A = CO<sub>2</sub>R, CONR<sub>1</sub>R<sub>2</sub>, CH<sub>2</sub>OR<sub>3</sub>, CH<sub>2</sub>NR<sub>4</sub>R<sub>5</sub>; R = H, cationic moiety, or CO<sub>2</sub>R = ophthalmically acceptable ester moiety; R<sub>1</sub>, R<sub>2</sub> = H, alkyl; R<sub>3</sub> = H, acyl, alkyl; R<sub>4</sub>, R<sub>5</sub> = H, acyl, alkyl, if one of R<sub>4</sub>, R<sub>5</sub> = acyl then the other = H or alkyl; n = 0, 2; L = OR<sub>6</sub> in the  $\alpha$  configuration where R<sub>6</sub> = H, alkyl, acyl; R<sub>7</sub> = H, alkyl, acyl; D, D<sub>1</sub> = H, OR<sub>8</sub>, R<sub>8</sub> = H, alkyl, acyl; X = (CH<sub>2</sub>)<sub>m</sub>, (CH<sub>2</sub>)<sub>m</sub>O, m = 1-6; Y = (un)substituted phenyl; XY = (CH<sub>2</sub>)<sub>p</sub>Y<sub>1</sub>; p = 0-6; W = CH<sub>2</sub>, O, S, SO, SO<sub>2</sub>, NR<sub>9</sub>, CH:CH, CH<sub>2</sub>O, CH<sub>2</sub>S, CH<sub>2</sub>SO, CH<sub>2</sub>SO<sub>2</sub>, CH:N, CH<sub>2</sub>NR<sub>9</sub>; R<sub>9</sub> = H, alkyl, acyl; Z = H, alkyl, alkoxy, acyl, acyloxy, halo, trihalomethyl, amino, alkylamino, acylamino, OH) were prepared for treatment of glaucoma and ocular hypertension. Thus, the diol II underwent tetrahydropyranylation, reduction and Wittig reaction with Ph<sub>3</sub>P+CH<sub>2</sub>OMe Cl<sup>-</sup> followed by cyclization to give the corresponding lactol, which underwent Wittig reaction with Ph<sub>3</sub>P+CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>H Br<sup>-</sup> to give the tetranorprostadienoic acid III. Ophthalmic formulations containing 0.001% III were prepared.

ST prostaglandin prepn ocular hypotensive; glaucoma treatment prostaglandin

IT Antiglaucoma agents  
 (preparation of cis- $\Delta$ 4 analogs of prostaglandins as ocular hypotensives)

- IT Prostaglandins  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of cis-Δ4 analogs of prostaglandins as ocular hypotensives)
- IT **192992-28-2P** 208112-13-4P 208115-11-1P 208180-50-1P  
 208180-52-3P 208180-54-5P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of cis-Δ4 analogs of prostaglandins as ocular hypotensives)
- IT 110-87-2, 3,4-Dihydro-2H-pyran 4009-98-7 17857-14-6 39746-01-5  
 53273-61-3 53872-60-9 54094-19-8 178454-81-4 192991-95-0  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (preparation of cis-Δ4 analogs of prostaglandins as ocular hypotensives)
- IT 39746-00-4P 71358-54-8P 84786-80-1P 105674-66-6P 130386-85-5P  
 192992-22-6P 192992-23-7P **192992-24-8P** **192992-25-9P**  
 208111-89-1P 208111-90-4P 208111-91-5P 208111-92-6P 208111-93-7P  
 208111-94-8P 208111-96-0P 208111-97-1P 208114-21-0P 208114-22-1P  
 208114-40-3P 208114-41-4P 208114-42-5P 208114-43-6P 208114-44-7P  
 208114-45-8P 208114-46-9P 208114-47-0P 208180-17-0P 208180-18-1P  
 208180-19-2P 208180-20-5P 208180-21-6P 208180-22-7P 208180-25-0P  
 208180-26-1P 208180-27-2P 208180-28-3P 208180-29-4P 208180-30-7P  
 208180-34-1P 208180-35-2P 208180-37-4P 208180-62-5P 208252-64-6P  
 208252-65-7P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of cis-Δ4 analogs of prostaglandins as ocular hypotensives)
- IT **192992-28-2P**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of cis-Δ4 analogs of prostaglandins as ocular hypotensives)
- RN 192992-28-2 HCAPLUS  
 CN L-altro-Oct-3-enitol, 5,8-anhydro-1-O-(3-chlorophenyl)-3,4,6-trideoxy-6-  
 [(3Z)-7-(1-methylethoxy)-7-oxo-3-heptenyl]-, (3E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).  
 Double bond geometry as shown.



L11 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1998:323138 HCAPLUS

Searched by P. Ruppel

DN 129:19683  
 ED Entered STN: 30 May 1998  
 TI Use of a combination of carbonic anhydrase inhibitors and prostaglandins for treating glaucoma  
 IN Dean, Thomas R.; May, Jesse A.  
 PA Alcon Laboratories, Inc., USA; Dean, Thomas R.; May, Jesse A.  
 SO PCT Int. Appl., 22 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM A61K031-557  
 ICS A61K031-54  
 CC 63-6 (Pharmaceuticals)  
 Section cross-reference(s): 1  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9819680	A1	19980514	WO 1997-US15793	19970905
W: AU, CA, JP, MX, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9742573	A1	19980529	AU 1997-42573	19970905
AU 734789	B2	20010621		
EP 948333	A1	19991013	EP 1997-940895	19970905
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001504100	T2	20010327	JP 1998-521363	19970905
MX 9904069	A	20000531	MX 1999-4069	19990430
PRAI US 1996-29538P	P	19961101		
WO 1997-US15793	W	19970905		

AB Compns. for treating persons suffering from glaucoma or ocular hypertension consist of prostaglandins and carbonic anhydrase inhibitors. Thus, an ophthalmic composition (pH 7.1) contained brinzolamide 1.0, (+)-isopropylfluprostenol 0.005, HPMC 0.5, dibasic sodium phosphate 0.2, disodium edetate 0.01, NaCl 0.8, benzalkonium chloride 0.01, and Cremaphor 0.1%, and purified water qs.  
 ST antiglaucoma prostaglandin carbonic anhydrase inhibitor  
 IT Antiglaucoma agents  
 (carbonic anhydrase inhibitors and prostaglandins for treatment of glaucoma)  
 IT Prostaglandins  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (carbonic anhydrase inhibitors and prostaglandins for treatment of glaucoma)  
 IT Drug delivery systems  
 (ophthalmic; carbonic anhydrase inhibitors and prostaglandins for treatment of glaucoma)  
 IT 138890-62-7, Brinzolamide 157283-68-6 192992-28-2  
 207670-11-9  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (carbonic anhydrase inhibitors and prostaglandins for treatment of glaucoma)  
 IT 9001-03-0, Carbonic anhydrase  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (inhibitors; carbonic anhydrase inhibitors and prostaglandins for treatment of glaucoma)  
 RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Alcon Lab Inc; EP 0590786 A 1994 HCAPLUS
- (2) Alcon Lab Inc; WO 9723223 A 1997 HCAPLUS
- (3) Alcon Laboratories Inc; EP 0667160 A 1995 HCAPLUS
- (4) Alcon Laboratories Inc; US 5378703 A 1995 HCAPLUS
- (5) Bishop, J; US 5510383 A 1996 HCAPLUS
- (6) Hoyng; SURVEY OF OPHTHALMOLOGY 1997, V41(S2), PS93
- (7) Merck & Co; CN 1075634 A 1993
- (8) Merck & Co; Ophthalmic Compositions Comprising Combinations of a Carbonic Anhydrase Inhibitor and a Prostaglandin or Prostaglandin Derivative 1993
- (9) Pfeiffer, N; CURRENT OPINION IN OPHTHALMOLOGY 1994, V5(2), P20
- (10) Ueno Seiyaku Oyo Kenkyujo Kk; EP 0501678 A 1992 HCAPLUS
- (11) Von der Eltz; PHARMAZEUTISCHE ZEITUNG 1996, V141(8), P11 HCAPLUS

IT 192992-28-2

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

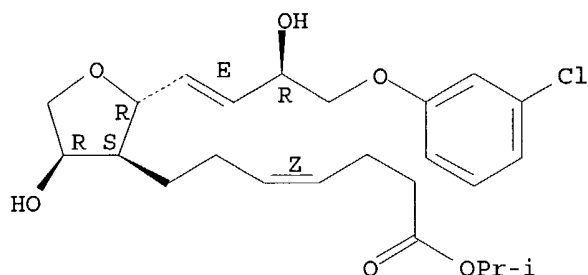
(carbonic anhydrase inhibitors and prostaglandins for treatment of glaucoma)

RN 192992-28-2 HCAPLUS

CN L-altro-Oct-3-enitol, 5,8-anhydro-1-O-(3-chlorophenyl)-3,4,6-trideoxy-6-[(3Z)-7-(1-methylethoxy)-7-oxo-3-heptenyl]-, (3E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

Double bond geometry as shown.



L11 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:503170 HCAPLUS

DN 127:135678

ED Entered STN: 09 Aug 1997

TI Preparation of substituted tetrahydrofuran analogs of prostaglandins as ocular hypotensives

IN Selliah, Robert D.; Hellberg, Mark R.; Klimko, Peter G.; Sallee, Verney L.; Zinke, Paul W.

PA Alcon Laboratories, Inc., USA; Selliah, Robert D.; Hellberg, Mark R.; Klimko, Peter G.; Sallee, Verney L.; Zinke, Paul W.

SO PCT Int. Appl., 64 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K031-557

ICS C07D307-18; C07D307-20; C07D307-80; C07D407-06

CC 26-3 (Biomolecules and Their Synthetic Analogs)

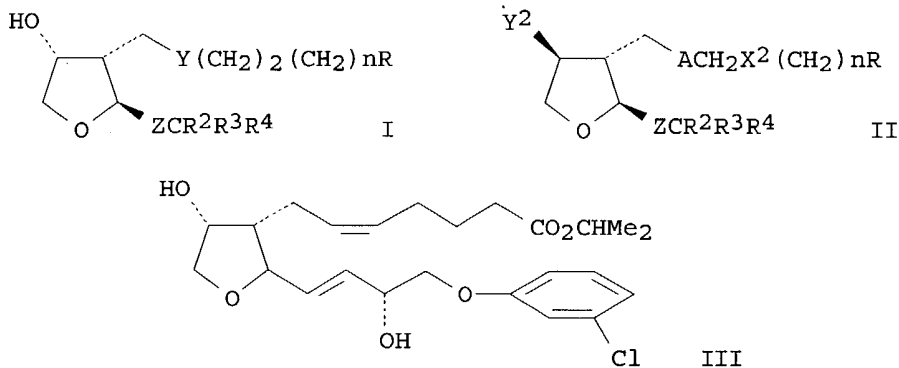
Section cross-reference(s): 1, 63

FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 9723223 A1 19970703 WO 1996-US17900 19961112  
W: AU, CA, CN, JP, MX, US  
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE  
CA 2236582 AA 19970703 CA 1996-2236582 19961112  
AU 9676106 A1 19970717 AU 1996-76106 19961112  
AU 714272 B2 19991223  
EP 869794 A1 19981014 EP 1996-938819 19961112  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI  
CN 1205638 A 19990120 CN 1996-199181 19961112  
JP 3032302 B2 20000417 JP 1997-523627 19961112  
US 5994397 A 19991130 US 1997-809920 19970404  
US 6025392 A 20000215 US 1998-109852 19980702  
US 6197812 B1 20010306 US 1999-440248 19991115  
US 2001029265 A1 20011011 US 2001-800179 20010306  
US 6369102 B2 20020409  
PRAI US 1995-9866P P 19951222  
WO 1996-US17900 W 19961112  
US 1997-809920 A2 19970404  
US 1999-440248 A1 19991115  
OS MARPAT 127:135678  
GI



AB Prostaglandin THF analogs I and II [R = CO<sub>2</sub>R<sub>1</sub>, CONR<sub>7</sub>R<sub>8</sub>, CH<sub>2</sub>OR<sub>9</sub>, CH<sub>2</sub>NR<sub>10</sub>R<sub>11</sub>; R<sub>1</sub> = H, cationic salt moiety; R<sub>7</sub> = R<sub>8</sub> = H, alkyl; R<sub>9</sub> = R<sub>10</sub> = R<sub>11</sub> = H, acyl, alkyl; Y = (Z)-CH<sub>2</sub>CH:CH, (Z)-CH:CHCH<sub>2</sub>, (CH<sub>2</sub>)<sub>3</sub>; Z = (E)-CH:CH, (CH<sub>2</sub>)<sub>2</sub>, C.tplbond.C; Y<sub>2</sub> = halogen, alkoxy; X<sub>2</sub> = O, S, CH<sub>2</sub>; A = (Z)-CH:CH, (CH<sub>2</sub>)<sub>2</sub>, C.tplbond.C; R<sub>2</sub> = R<sub>3</sub> = H, F, OH; R<sub>2</sub>R<sub>3</sub> = O, protected carbonyl; R<sub>4</sub> = cyclohexyl, alkyl] were prepared for use in treating glaucoma and ocular hypertension (no data). Thus, prostaglandin analog III was prepared in a multistep synthesis starting from 1,2-O-isopropylidene-α-D-xylofuranose.

ST prostaglandin THF analog prepn ocular hypertension; glaucoma agent  
prostaglandin THF analog prepn; oxaprostaglandin prepn glaucoma agent  
ocular hypertension

IT Antihypertensives  
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(ocular; preparation of substituted THF analogs of prostaglandins as ocular hypotensives)

IT Antiglaucoma agents

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substituted THF analogs of prostaglandins as ocular hypotensives)

IT Prostaglandins

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prostanoids; preparation of substituted THF analogs of prostaglandins as ocular hypotensives)

IT 98-88-4, Benzoyl chloride 108-98-5, Thiophenol, reactions 867-13-0, Triethylphosphonoacetate 4009-98-7, (Methoxymethyl)triphenylphosphonium chloride 17814-85-6, (4-Carboxybutyl)triphenylphosphonium bromide 17857-14-6, (3-Carboxypropyl)triphenylphosphonium bromide 20031-21-4 29921-57-1, Isopropyl bromoacetate 40665-94-9 58009-66-8 88738-78-7  
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of substituted THF analogs of prostaglandins as ocular hypotensives)

IT 6022-96-4P 6698-46-0P 58399-68-1P 77772-47-5P 80923-96-2P  
192991-91-6P 192991-92-7P 192991-93-8P 192991-94-9P 192991-95-0P  
192991-98-3P 192992-00-0P 192992-02-2P **192992-03-3P**  
**192992-04-4P 192992-05-5P** 192992-06-6P 192992-07-7P  
192992-08-8P 192992-09-9P 192992-10-2P 192992-11-3P 192992-12-4P  
192992-13-5P 192992-14-6P 192992-15-7P 192992-16-8P 192992-17-9P  
192992-18-0P 192992-19-1P 192992-20-4P 192992-21-5P 192992-22-6P  
192992-23-7P **192992-24-8P 192992-25-9P** 192992-30-6P  
193075-40-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of substituted THF analogs of prostaglandins as ocular hypotensives)

IT **113428-35-6P 192992-26-0P** 192992-27-1P  
**192992-28-2P** 192992-29-3P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substituted THF analogs of prostaglandins as ocular hypotensives)

IT **192992-03-3P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

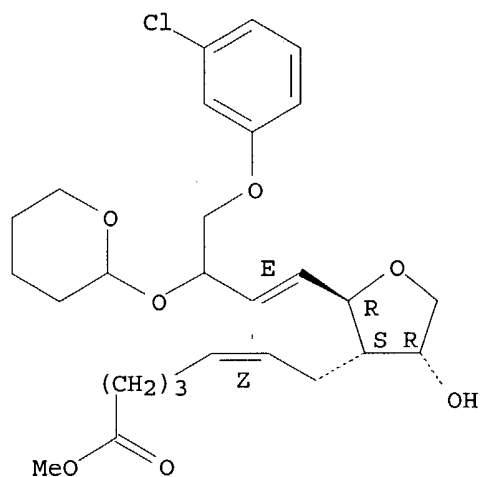
(preparation of substituted THF analogs of prostaglandins as ocular hypotensives)

RN 192992-03-3 HCAPLUS

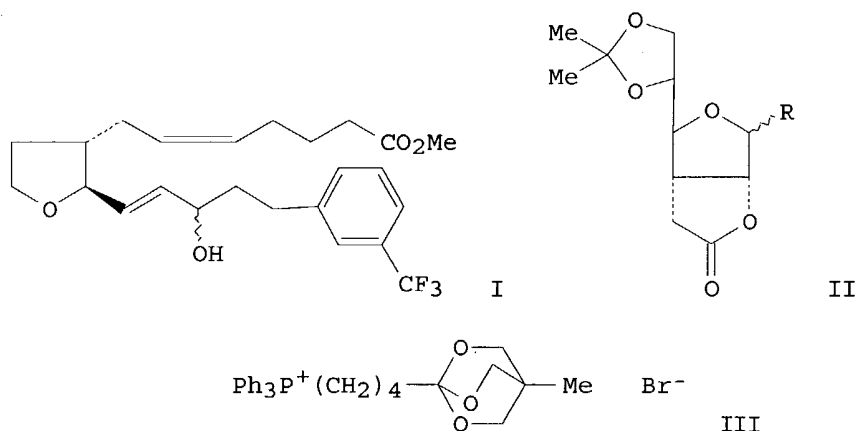
CN D-ribo-Oct-5-enitol, 1,4-anhydro-8-O-(3-chlorophenyl)-3,5,6-trideoxy-3-[(2Z)-7-methoxy-7-oxo-2-heptenyl]-7-O-(tetrahydro-2H-pyran-2-yl)-, (5E,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L11 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1988:131340 HCAPLUS  
 DN 108:131340  
 ED Entered STN: 15 Apr 1988  
 TI Synthesis of methyl (5Z,13E) (15S)-9 $\alpha$ -acetoxy-15-hydroxy-17-(3-trifluoromethylphenyl)-11-oxa-18,19,20-trinorprosta-5,13-dienoate  
 AU Verdoorn, Gerhard H.; Holzapfel, Cedric W.; Koekemoer, Johannes M.  
 CS Dep. Chem., Rand Afrikaans Univ., Johannesburg, 2000, S. Afr.  
 SO South African Journal of Chemistry (1987), 40(2), 134-8  
 CODEN: SAJCDG; ISSN: 0379-4350  
 DT Journal  
 LA English  
 CC 26-3 (Biomolecules and Their Synthetic Analogs)  
 GI



AB The title compound (I) was prepared from D-glucose. A key step in the synthesis was the deoxygenation of the furanose II (R = OH) by reaction with MeSO<sub>2</sub>Cl and NaBH<sub>3</sub>CN reduction of II (R = Cl). An improved method for the introduction of the  $\omega$ -side chain utilizes the orthoester III.

ST oxatrinorprostadienoate; prostaglandin oxa  
IT Prostaglandins  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(oxatrinorprostadienoates, preparation of)  
IT 779-89-5, 3-Trifluoromethylcinnamic acid  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(hydrogenation of)  
IT 58399-55-6  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(hydrolysis of)  
IT 70783-99-2P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and Wittig reaction of, with tetrahydrofurancarboxaldehyde)  
IT 113531-01-4P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and acetylation of)  
IT 585-50-2P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and chlorination of)  
IT 113331-70-7P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and dehydroxylation of)  
IT 113331-72-9P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and deisopropylidenation of)  
IT 113331-74-1P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and hydrolysis of)  
IT 113331-78-5P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and oxidation of)  
IT 113331-71-8P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and reaction of, with carboxybutyltriphenylphosphonium bromide)  
IT 113331-73-0P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and reaction of, with dioxabicyclooctanol)  
IT 113331-75-2P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and reaction of, with methoxide)  
IT 455-03-8P, 3-(3-Trifluoromethylphenyl)propionyl chloride  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and reaction of, with methylphosphonate)  
IT 113331-77-4P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and reaction of, with triphenylphosphine)  
IT 113331-76-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)

(preparation and rearrangement of)

IT 101069-36-7P **113331-79-6P**  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and reduction of)

IT **113331-80-9P 113428-35-6P**  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

IT 3143-02-0, 3-Hydroxymethyl-3-methyloxetane  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reaction of, with bromovaleryl chloride)

IT 17814-85-6, 4-Carboxybutyltriphenylphosphonium bromide  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reaction of, with dioxabicyclooctanol)

IT 4509-90-4, 5-Bromovaleryl chloride  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reaction of, with hydroxymethylmethyloxetane)

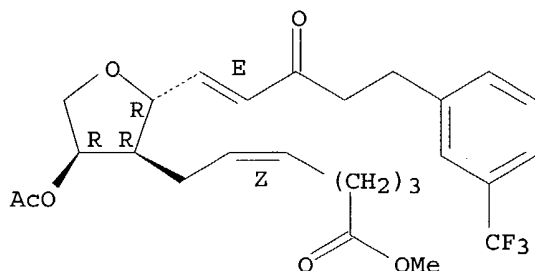
IT 756-79-6, Dimethyl methylphosphonate  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reaction of, with trifluoromethylphenylpropionyl chloride)

IT **113331-79-6P**  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and reduction of)

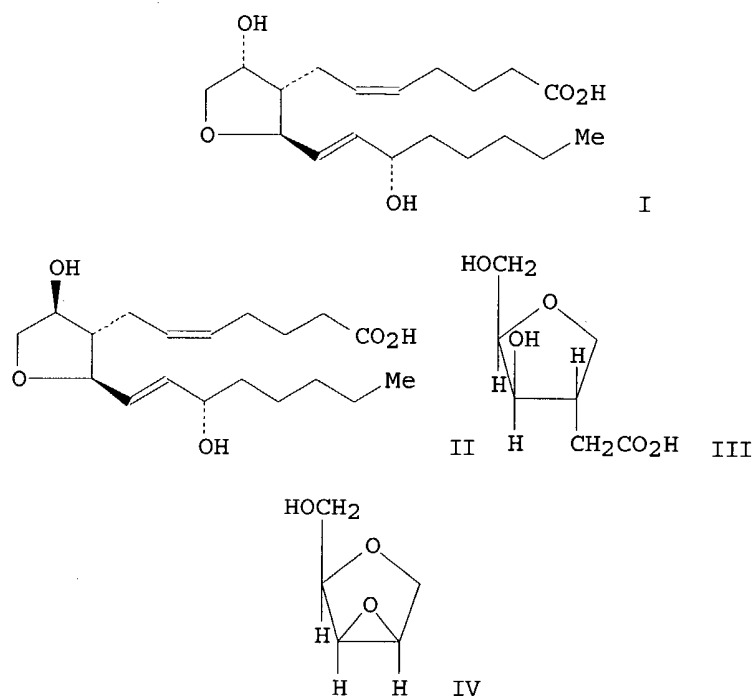
RN 113331-79-6 HCAPLUS

CN 5-Heptenoic acid, 7-[4-(acetyloxy)tetrahydro-2-[3-oxo-5-[3-(trifluoromethyl)phenyl]-1-pentenyl]-3-furanyl]-, methyl ester, [2R-[2 $\alpha$ (E),3 $\beta$ (Z),4 $\beta$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



L11 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1986:186178 HCAPLUS  
 DN 104:186178  
 ED Entered STN: 01 Jun 1986  
 TI Total synthesis of 11-oxaprostaglandin F2 $\alpha$  and F2 $\beta$   
 AU Hanessian, Stephen; Guindon, Yvan; Lavallee, Pierre; Dextraze, Pierre  
 CS Dep. Chem., Univ. Montreal, Montreal, QC, H3C 3V1, Can.  
 SO Carbohydrate Research (1985), 141(2), 221-38  
 CODEN: CRBRAT; ISSN: 0008-6215  
 DT Journal  
 LA English  
 CC 26-3 (Biomolecules and Their Synthetic Analogs)  
 Section cross-reference(s): 33  
 OS CASREACT 104:186178  
 GI



- AB Title compds. I and II and their C-15 epimers were synthesized from 1,4-anhydro-D-glucitol. Also prepared were chiral THF derivs. such as III and IV. I and II did not show smooth-muscle contracting ability.
- ST anhydroglucitol oxa prostaglandin synthon; glucitol anhydro prostaglandin synthon
- IT Synthons  
(anhydroglucitol, for prostaglandin oxa analogs)
- IT Prostaglandins  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(analog, PGF2 oxa, total synthesis of, from anhydroglucitol)
- IT 36969-89-8  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(Wittig condensation of, in synthesis of oxa prostaglandins)
- IT 105-53-3  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(alkylation with, in synthesis of oxa prostaglandins from anhydroglucitol)
- IT 55730-76-2P 101144-12-1P 101144-18-7P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and alkylation with di-Et malonate)
- IT 55285-66-0P 55730-81-9P 101069-33-4P 101069-52-7P  
101069-55-0P 101144-16-5P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and borohydride reduction of)
- IT 55730-79-5P 101069-39-0P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and conversion into acetonide)

IT 55730-74-0P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and conversion into epoxide)

IT 101069-30-1P 101069-36-7P 101069-45-8P 101069-62-9P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and deprotection of)

IT 101069-34-5P 101069-44-7P 101144-06-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and desilylation of)

IT 101069-35-6P 101069-43-6P 101069-50-5P 101069-51-6P 101069-60-7P  
101069-61-8P 101144-15-4P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and esterification of)

IT 101144-07-4P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and hydride reduction of)

IT 101069-27-6P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and hydrogenation of)

IT 101069-26-5P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and oxidation to ketone)

IT 101069-48-1P 101069-49-2P 101069-58-3P 101069-59-4P 101144-14-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and partial decarboxylation of)

IT 59286-02-1P 101069-31-2P 101069-37-8P 101069-46-9P 101069-54-9P  
101222-38-2P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and periodate oxidation of)

IT 101069-29-8P 101069-42-5P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and reaction with (carboxybutyl)triphenylphosphonium bromide)

IT 58399-68-1P 101069-32-3P 101069-38-9P 101069-47-0P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and reaction with (tributylphosphoranylidene)heptanone)

IT 101125-99-9P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and reaction with [(ethoxycarbonyl)methylene]triphenylphosphorane)

IT 55730-77-3P 55730-78-4P 61876-91-3P 61914-86-1P 101069-56-1P  
101069-57-2P 101144-08-5P 101144-09-6P 101144-13-2P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and saponification of)

IT 101069-41-4P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and silylation of)

IT 101069-28-7P  
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and use in synthesis of oxa prostaglandins)

IT 55730-73-9P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation and use of, in synthesis of oxa prostaglandins)

IT 55730-75-1P 58399-69-2P 101069-40-3P 101069-53-8P 101069-63-0P  
 101126-00-5P 101144-17-6P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

IT 25952-53-8  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reaction of, with anhydroglucitol derivative)

IT 27299-12-3P  
 RL: PREP (Preparation)  
 (starting material for synthesis of oxa prostaglandins)

IT 58399-72-7P 58437-46-0P 101144-10-9P 101144-11-0P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (total synthesis of, from anhydroglucitol)

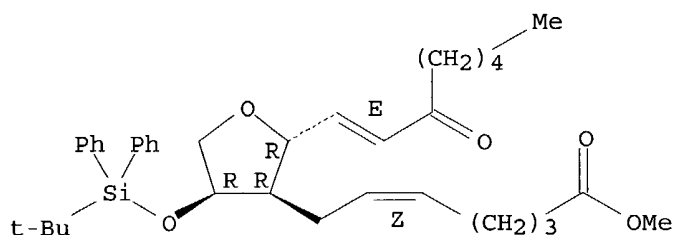
IT 1099-45-2 17814-85-6 35563-52-1  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (use of, in synthesis of oxa prostaglandins)

IT 101069-33-4P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and borohydride reduction of)

RN 101069-33-4 HCAPLUS

CN 5-Heptenoic acid, 7-[4-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]tetrahydro-2-(3-oxo-1-octenyl)-3-furanyl]-, methyl ester, [2R-[2 $\alpha$ (E),3 $\beta$ (Z),4 $\beta$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.

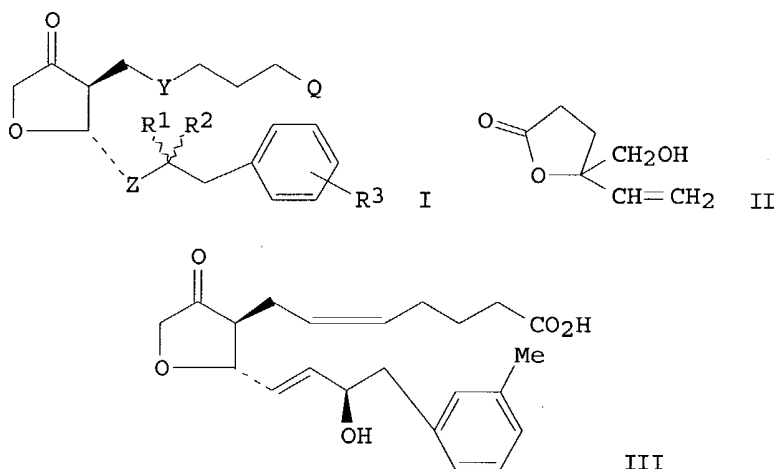


L11 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1978:405999 HCAPLUS  
 DN 89:5999  
 ED Entered STN: 12 May 1984  
 TI 11-Deoxy-11-oxaprostaglandin compounds  
 IN Corey, Elias James; Egger, James Frederick  
 PA Pfizer Inc., USA  
 SO Ger. Offen., 49 pp.  
 CODEN: GWXXBX  
 DT Patent  
 LA German  
 IC C07D307-32  
 CC 24-4 (Alicyclic Compounds)  
 Section cross-reference(s): 27, 63  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	DE 2739277	A1	19780316	DE 1977-2739277	19770831
	DE 2739277	C2	19820609		
	JP 53037653	A2	19780406	JP 1977-109398	19770910
	JP 57055719	B4	19821125		
	BE 858682	A1	19780314	BE 1977-180893	19770914
	DK 7704083	A	19780316	DK 1977-4083	19770914
	NL 7710065	A	19780317	NL 1977-10065	19770914
	NL 169739	B	19820316		
	NL 169739	C	19820816		
	FR 2364912	A1	19780414	FR 1977-27747	19770914
	FR 2364912	B1	19801003		
	GB 1539364	A	19790131	GB 1977-38389	19770914
PRAI	US 1976-723604		19760915		
GI					



AB I (Q = carboxy or tetrazolyl, R1,R2 = H, OH; R3 = H, Cl, F, Me, MeO, CF3, A = CH2CH2 or cis-CH:CH, and Z = CH2CH2 or trans CH:CH) were prepared. Thus, 1,2:5,6-diisopropylidene-D-mannitol was treated with Pb(OAc)4 to give YCHO (Y = 2,2-dimethyl-1,3-dioxolan-4-yl), which with (MeO)2P(O)CH2CO2Me gave YCH:CHCO2Me; this was vinyllated and lactonized to give II, which was incorporated into conventional prostaglandin synthesis procedures to give ent-prostaglandin analogs, e.g., III.

ST prostaglandin oxa ent

IT Prostaglandins

RL: RCT (Reactant); RACT (Reactant or reagent)  
(11-oxa analogs)

IT 1707-77-3

RL: RCT (Reactant); RACT (Reactant or reagent)  
(lead tetraacetate cleavage of)

IT 917-57-7

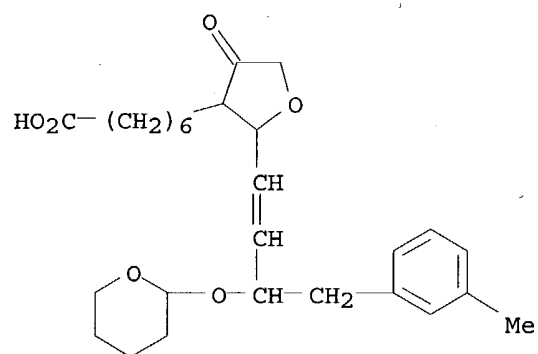
RL: RCT (Reactant); RACT (Reactant or reagent)  
(metalation-addition reaction of, with dioxolanylacrylate derivative)

IT 66601-86-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and borohydride reduction of)

IT 66601-88-5P 66674-02-0P

- RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and hydride reduction of)
- IT 66601-92-1P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and hydrogenation of)
- IT 66601-91-0P 66674-04-2P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and hydrolysis or hydrogenation of)
- IT 66601-82-9P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and metalation-addition reaction with vinylolithium)
- IT 58399-67-0P 58399-67-0P 66601-90-9P 66674-03-1P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and oxidation of)
- IT 66601-84-1P 66601-85-2P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and oxidation with 3-chloroperbenzoic acid)
- IT 66601-87-4P 66674-01-9P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and protection with dihydropyran)
- IT 66601-89-6P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and reaction with (4-carboxybutyl)triphenylphosphonium bromide)
- IT 66673-99-2P 66674-00-8P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and reaction with di-Me [2-oxo-3-(3-methylphenyl)propyl]phosphonate)
- IT 15186-48-8P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and reaction with tri-Me phosphonoacetate)
- IT 66601-83-0P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and use in oxaprostaglandin synthesis)
- IT 66601-93-2P 66674-05-3P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)
- IT 5927-18-4  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with isopropylideneglyceraldehyde)
- IT 17814-85-6 61263-05-6  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(use of, in oxaprostaglandin synthesis)
- IT 66601-92-1P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and hydrogenation of)
- RN 66601-92-1 HCAPLUS  
CN 3-Furanheptanoic acid, tetrahydro-2-[4-(3-methylphenyl)-3-[(tetrahydro-2H-pyran-2-yl)oxy]-1-butenyl]-4-oxo-, [2S-[2 $\alpha$ , (1E,3R\*),3 $\beta$ ]]- (9CI)  
(CA INDEX NAME)



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